(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 December 2000 (21.12.2000)

PCT

(10) International Publication Number
WO 00/76663 A1

(51) International Patent Classification[7]: B01L 3/00, G01N 21/25, 35/02

(21) International Application Number: PCT/GB00/02251

(22) International Filing Date: 9 June 2000 (09.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9913561.8 10 June 1999 (10.06.1999) GB

(71) Applicant *(for all designated States except US)*: **PROVALIS DIAGNOSTICS LIMITED** [GB/GB]; Newtech Square, Deeside Industrial Park, Deeside, Flintshire CH5 2NT (GB).

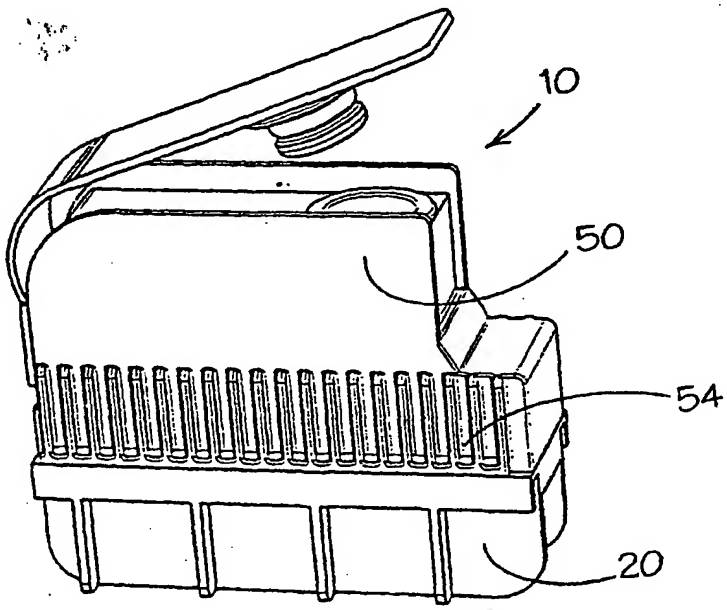
(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **ANDREWES, David** [GB/GB]; 5 Ridgeway Road, Farnham, Surrey GU9 8NN (GB). **O'DELL, John, Anthony** [GB/GB]; 24 Halford Road, Fulham, London SW6 1JT (GB). **STEVENSON, Anthony** [GB/GB]; 4 Beaumont Close, Chester CH4 8PT (GB). **CURTIS, John** [GB/GB]; Balderton House, Balderton, Chester CH4 9FL (GB). **GRAY, Adrian, Richard** [GB/GB]; West End House, Vaughans Lane, Chester CH3 5XF (GB). **VESSEY, John, Philip** [GB/GB]; Canna, Forest Road, East Horsley, Surrey KT24 5BT (GB). **FERNANDO, Felix** [GB/GB]; 24 Tudor Close, Wokingham, Berks RG40 2LU (GB). **CRESWELL, Mark** [GB/GB]; 11 Main Road, Broughton, Chester CH4 0NW (GB). **PERCIVAL, David, Alan** [GB/GB]; 4 Overlea Drive, Hawarden, Flintshire CH5 3HS (GB). **ATTRIDGE, John, Worthington** [GB/GB]; Oaksbridge, Send Marsh Road, Ripley, Surrey CH23 6JR (GB).

(74) Agent: **W.P. THOMPSON & CO.**; Coopers Building, Church Street, Liverpool L1 3AB (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,

[Continued on next page]

(54) Title: APPARATUS, INSTRUMENT AND DEVICE FOR CONDUCTING AN ASSAY



(57) Abstract: The present invention relates to an apparatus, instrument and device for conducting an assay. The apparatus comprises a first inlet (12), a second inlet (14) and an inlet port (16) accommodating a filter or binder retaining means, wherein said inlet port is moveable relative to first and second inlets such that the inlet port can be brought into liquid communication with each inlet as required.

WO 00/76663 A1

DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) **Designated States** *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

5/prts

DESCRIPTION

APPARATUS, INSTRUMENT & DEVICE FOR CONDUCTING AN ASSAY

The present invention relates to an apparatus, instrument and device for conducting an assay. More particularly is relates to a device suitable for use in assaying analyses, for example glycated protein, in a sample, such as for example, blood.

The applicant has devised an apparatus, instrument and device for conducting an assay as disclosed in PCT/GB98/033586. The apparatus comprises a first inlet, a second inlet, and an inlet port, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each inlet in turn as required, said inlet port accommodating a filter means or a binder retaining means.

In use a sample is separated into a first component fraction and a second component fraction and the component fractions are assayed to determine the presence of one or more analyses in said sample fractions.

The component fractions are read in an instrument comprising a microprocessor operable via a keypad, one or more light emitters and one or more light detectors, a display and driver, an analogue to digital converter and means for connecting the instrument to a power source.

The apparatus takes the form of a carousel. It comprises a base portion having a plurality of chambers including first and second inlets, and a top portion which together with the base portion forms the carousel. A funnel portion comprising an inlet port is in

liquid communication with said inlets.

In use the assay reagents are opened and added sequentially by the user such as a doctor or patient.

It would be desirable to provide an apparatus, instrument and device for conducting an assay which is simpler to use and is less prone to user error. It would also be advantageous if such an apparatus could be produced cheaply.

According to a first aspect of the present invention there is provided an apparatus, for use in an assay in which a sample is presented to an instrument, comprising a first inlet, a second inlet and an inlet port, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each inlet in turn as required, said inlet port accommodating a filter means or a binder retaining means characterised in that said inlet port is brought into liquid communication with each inlet in turn along a linear path.

Preferably the apparatus takes the form of a cartridge.

Preferably the cartridge comprises a first component including the at least first and second inlets, which are or include optical chambers; a second component or components comprising a sample receiving chamber and at least one other chamber, said at least one other chamber containing an eluting medium; and a third component comprising said inlet port. Said third component is slidably disposed below the receiving chambers in said first component and above the optical chambers in the second component.

Preferably the third component forms a seal between the chamber of the second

component so that liquids stored or pre-loaded into the chambers are only released when the inlet port formed therein is aligned with the chambers. Alignment is achieved by sliding the third component along a linear path. Additional sealing means could, however, be deployed to prevent leakage.

Preferably the third component is provided with a handle or other means by which the component can be moved.

Preferably the apparatus is manufactured in a manner enabling easy filling of the chambers. Thus it is preferred that the second component comprises a resilient component and a cover. Preferably the resilient component comprises a plug closure.

To assemble and fill the apparatus the various components are assembled as follows:

1. The resilient component comprising, for example, three chambers is placed in the cover,

2. The plug closure pivots into place,

3. The assay liquids are poured into the 1st chamber, 2nd chamber and 3rd chamber,

4. The filter and/or binding means is located in the inlet port of the 3rd component and this is slid into the 2nd component,

5. The 1st component, including the 1st and 2nd inlets comprising optical chambers, is clipped into place, thus forming the cartridge.

Preferably the second component comprises a channel within which the 3rd

component slides.

The easier it is to use a product the more acceptable it is. By following a linear path the sequence of operations can be simplified to:

1. Unpack the cartridge;
2. Rest the cartridge on a surface and pull open the closure;
3. Take, for example, a blood sample using a loop;
4. Place the blood sample into the open chamber;
5. Replace the plug closure;
6. Shake the cartridge;
7. Insert the cartridge into an instrument.

The cartridge is designed to be inserted into the instrument in one orientation and is provided with locator lugs to ensure correct orientation.

According to a further aspect of the present invention there is provided an instrument, for reading a sample presented in an apparatus, comprising a microprocessor operable via a key pad, one or more light emitters and one or more light detectors, a display and driver, an analogue to digital converter, and means for connecting the instrument to a power source, characterised in that the instrument comprises an elongate track adapted to bring an apparatus into a reading position.

Preferably the instrument includes a filter for selecting a suitable wavelength.

According to yet a further aspect of the present invention there is provided a device comprising an apparatus and instrument of the invention.

The next series of steps are operated from the instrument. The instrument is designed such that at the completion of the testing the cartridge cannot be removed until returned to the start position. This is to seal the spent cartridge and to have the instrument ready for the next test.

The cartridge provides user simplicity. The cartridge benefits from the following features:

There is only one closure and this cannot be removed.

The first component, which is clear has a plurality of projecting fins on its side which give stability when loading the sample, and unsure correct orientation into the instrument and helps prevent fingerprinting the surface.

The filter is hidden, inaccessible and being totally enclosed is immune to violent shaking.

The liquids, their chambers and the filter slide surfaces are enclosed and are not easily contaminated.

In normal usage the user cannot unintentionally operate the cartridge until installed in the instrument.

In one embodiment the faces of the optical chambers can be curved.

The filter is fully aligned with the chamber apertures before air can enter. This means the product drops by gravity only when the chambers are fully aligned. The aim being fast emptying and agitation. The air tubes are positioned to allow this.

The disposable cartridge has only a few parts.

The cartridge benefits from a non-return snap together assembly.

The cartridge benefits from reduced size compared to a carousel, and can be easily packaged in multiples.

The construction means the cartridge is fully sealed for after-use disposal.

The construction allows for a possible reduction in instrument size.

The invention will be now described, by way of example only, with reference to the following figures in which:

Fig. 1 is a perspective view of a cartridge of the invention.

Fig. 2 is an exploded view showing the component parts of the cartridge of Fig. 1;

Fig. 3 is a cross section through the cartridge of Fig. 1; and

Figs. 4 to 7 show cross-sections of the cartridge in an instrument at various stages during an assay procedure.

Referring to Figs. 1 to 3 the apparatus 10 of the invention takes the form of a cartridge. It comprises a first inlet 12, a second inlet 14 and an inlet port 16. The inlet port 16 comprises a filter 18 capable of retaining a binder retaining means.

The cartridge is constructed from a number of component parts. A first component part 20 is made of a clear material, for example, plastics, most preferably acrylic, and houses optical chambers 12 and 14. An additional chamber 13 is disposed between optical chambers 12 and 14 and functions as a wash chamber.

A second component 30 comprises two parts, a resilient component 40 and a cover

50.

The resilient component 40 comprises an elongate channel 42 (partially obscured) into which a third component 60 is slidably mounted. The third component comprises an inlet port 16 in which is housed a filter and/or binder retaining means 18 and a handle 64.

To construct the cartridge 10 the resilient component 40, which is made of rubber, is placed into cover 50. The rubber component 40 comprises three openings 44, 45, 46, which extend into the elongate channel 42. These openings, which are closed to form sample receiving chambers 24, 25, 26 by slide component 60, house various assay liquids. In the case of an assay for determining glycated and non-glycated proteins in haemoglobin the resulting sample receiving chambers 24, 25, and 26 contain respectively,

1) a buffer and an amino phenylboronate agarose matrix,

2) a wash buffer, and

3) an eluting buffer.

Extending and pivoting from one end of the rubber component 40 is a closure lid 47 which seals an aperture 52 in the cover 50 which leads into the filling chamber 24. At the side of each chamber 24, 25 and 26 is an air relief tube 48 which co-operates with an aperture (not shown) in the slide 60 such that when the inlet port 16 is correctly aligned with each chamber 24, 25 and 26 the aperture is aligned with the associated air relief tube thereby causing an air lock to break thus causing release of the chamber contents through the filter into the inlet there below. The component 40 further comprises a plurality of mating members 49 which allow it to be connected to component parts 20 and 50.

The first component comprises windows 72 and 74 which are inset from the main

cartridge surface 76. By having the article windows inset and having projecting fins 78 on either side of the windows, fingerprints, can be avoided and the component strengthened. The second component 60 is preferably "I" shaped in cross section so that it can run against a number of surfaces ensuring a good sealing and preventing leakage from the respective chambers. It also has a handle 64 which can be held in a reading instrument; preferably on the track on which the cartridge runs.

The cover 50, has a toothed surface 54 which teeth provide a means by which the cartridge can be caused to move along a track 80 of a reading instrument.

To assemble and fill the cartridge the rubber component 40 is placed into the cover 50 and the plug closure 47 pivots to close aperture 52. The test liquids are then poured into the chambers 44, 45 and 46. The 3rd component slide 60, with filter 18 then slid into the channel 42 of the rubber component 40 thereby sealing the chamber 44, 45 and 46. The first component is then clipped into place thereby completing assembly.

The device is used in an assay as follows:

1) The cartridge is unpacked and the closure 47 opened.

2) A finger-prick blood sample is collected into a loop and placed into chamber 44 through aperture 52. The chamber comprises a buffer and an amino phenyl boronate (aPBA) agarose affinity matrix. The chamber is closed and the cartridge inverted several times, causing the red blood cells to be lysed thus liberating the haemoglobin.

3) The tube is left for approximately 60-90 seconds, with occasional inversion, during which the glycated haemoglobin present in the sample binds to the aPBA affinity

matrix.

4) During this time, the apparatus 10, which is designed to be disposable, is placed on the track 80 of an instrument which will read the samples and calculate and display the results (Fig. 4).

5) After about 60-90 seconds incubation, the inlet port 16 of the slide component is caused to move relative to the chambers 44, 45 and 46 and the corresponding chambers 12, 13, and 14. In fact the slide is held in position by locking handle 64 into a stop 82 on the track and the cartridge is caused to move along the track 80 by utilising the teeth 54 on the cover 50 to propel the cartridge.

6) When the inlet port 16 is aligned with the first inlet 12 and the first chamber 44 the first air relief tube 48 is caused to break releasing the contents of the first chamber 44 into contact with the filter 16. (Fig 5) The liquid contents of the chamber drain through the filter and are collected in the optical chamber 12. The aPBA affinity matrix, however, is too large to pass through the filter and therefore collects in the inlet port 16.

7) The liquid contents collect in the first optical chamber which contains the non-glycated haemoglobin present in the original sample, the aPBA affinity matrix collected in the inlet port 16 contains the glycated haemoglobin present in the original sample.

8) On completion of this first step, the instrument progresses to stage 2, which is accomplished by causing the cartridge to move along the track and stop at position 2 (Fig. 6). Again, under direction from the instrument the wash buffer from chamber 45 is released into chamber 13 via inlet port 16 and allowed to drain through. This step is to remove any

non-specifically bound non-glycated haemoglobin from the aPBA affinity matrix that may be present from step 1.

9) The instrument progresses to stage 3 and the contents of the chamber 46 is released into chamber 14 via inlet port 16. The elution buffer removes the glycated haemoglobin from the aPBA affinity matrix. (Fig. 7).

10) During the above the instrument spectrophotometrically measures the absorbance of both the non-glycated and the glycated haemoglobin fractions present in the two optical chambers. Using an algorithm built into the instruments software, the % glycated haemoglobin present in the original whole blood sample is calculated and displayed on the display.

11) The apparatus returns to its starting position, is disconnected from the instrument and is discarded as biohazardous waste. The instrument is then ready to perform the next test.

Whilst the invention has been described with reference to an assay for determining the % levels of glycated haemoglobin, the skilled man will appreciate that the number of inlets and chambers and the assay liquids will vary for other assay systems.

CLAIMS

1. An apparatus 10, for use in an assay in which a sample is presented to an instrument, comprising a first inlet 12, a second inlet 14 and an inlet port 16, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each inlet in turn as required, said inlet port accommodating a filter means or a binder retaining means 18 characterised in that said inlet port is brought into liquid communication with each inlet in turn along a linear path.

2. An apparatus as claimed in claim 1 which is a cartridge.

3. An apparatus as claimed in claim 1 or 2 comprising a first component 20 including the at least first and second inlets 12,14, which are or include optical chambers; a second component 30 or components 40,50 comprising a sample receiving chamber 44 and at least one other chamber 46, said at least one other chamber containing an eluting medium; and a third component 60 comprising said inlet port 16.

4. An apparatus as claimed in claim 3 wherein said third component is slidably disposed below the sample receiving chamber in said second component and above the optical chambers in the first component.

5. An apparatus as claimed in claim 3 or 4 in which the third component seals the sample receiving chamber of the second component so that liquids stored or pre-loaded into the chamber are only released when the inlet ports formed therein are aligned with the optical chambers in the first component.

6. An apparatus as claimed in claim 5 further comprising additional sealing means.

7. An apparatus as claimed in any of claims 3 to 6 in which the third component is provided with a handle or other means by which it can be moved.

8. An apparatus as claimed in any of claims 3 to 7 in which the second component comprises a resilient component and a cover.

9. An apparatus as claimed in claim 8, in which the resilient component comprises a plug closure.

10. An apparatus as claimed in any of claims 3 to 9 in which the second component comprises a channel within which the third component slides.

11. An apparatus as claimed in any of the preceding claims further comprising locator lugs to ensure correct orientation in a measuring instrument.

12. An apparatus as claimed in any of claims 3 to 11 further comprising a plurality of fins projecting from the first component.

13. An apparatus as claimed in any of the preceding claims in which the optical chambers are curved.

14. An apparatus as claimed in any of the preceding claims comprising air relief tubes.

15. An apparatus as claimed in any of claims 3 to 14 wherein the first component is made of a clear material.

16. An apparatus as claimed in any of claims 3 to 15 in which the second component comprises two parts, a resilient component and a cover.

17. An apparatus as claimed in any of claims 3 to 16 wherein the resilient

component comprises an elongate channel into which the third component is slidably mounted.

18. An apparatus as claimed in claim 14 wherein each air relief tube co-operates with an aperture in the slide such that when the inlet port is correctly aligned with each chamber the aperture is aligned with the associated air relief tube thereby causing an air lock to break thus causing release of the chamber contents through the filter into the inlet there below.

19. An apparatus as claimed in any of claims 3 to 18 wherein the first component comprises windows which are inset from the main apparatus surface.

20. An apparatus as claimed in any of claims 3 to 19 wherein the second component is "I" shaped in cross section.

21. An apparatus as claimed in any of the preceding claims wherein the apparatus has a toothed surface which teeth provide a means by which the apparatus can be caused to move along a track of a reading instrument.

22. An instrument for reading a sample presented in an apparatus, comprising a microprocessor operable via a key pad, one or more light emitters and one or more light detectors, a display and driver, an analogue to digital converter, and means for connecting the instrument to a power source, characterised in that the instrument comprises an elongate track adapted to bring an apparatus into a reading position.

23. An instrument as claimed in claim 22 further comprising a filter for selecting a suitable wavelength.

24. A device comprising an apparatus as claimed in any of claims 1 to 21 and an instrument as claimed in claims 22 and 23.

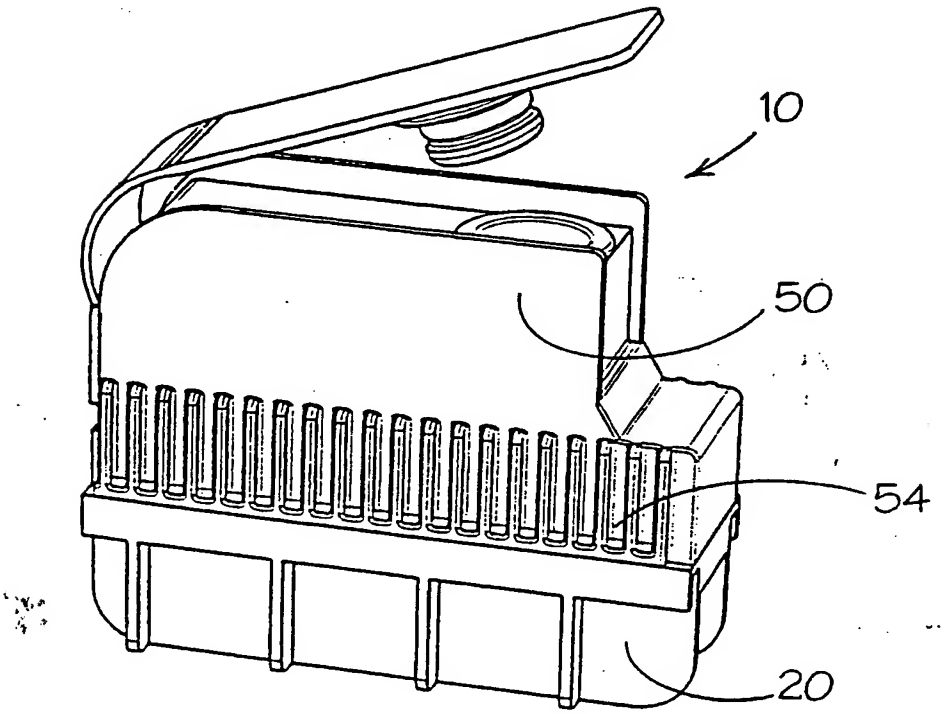


FIG. 1.

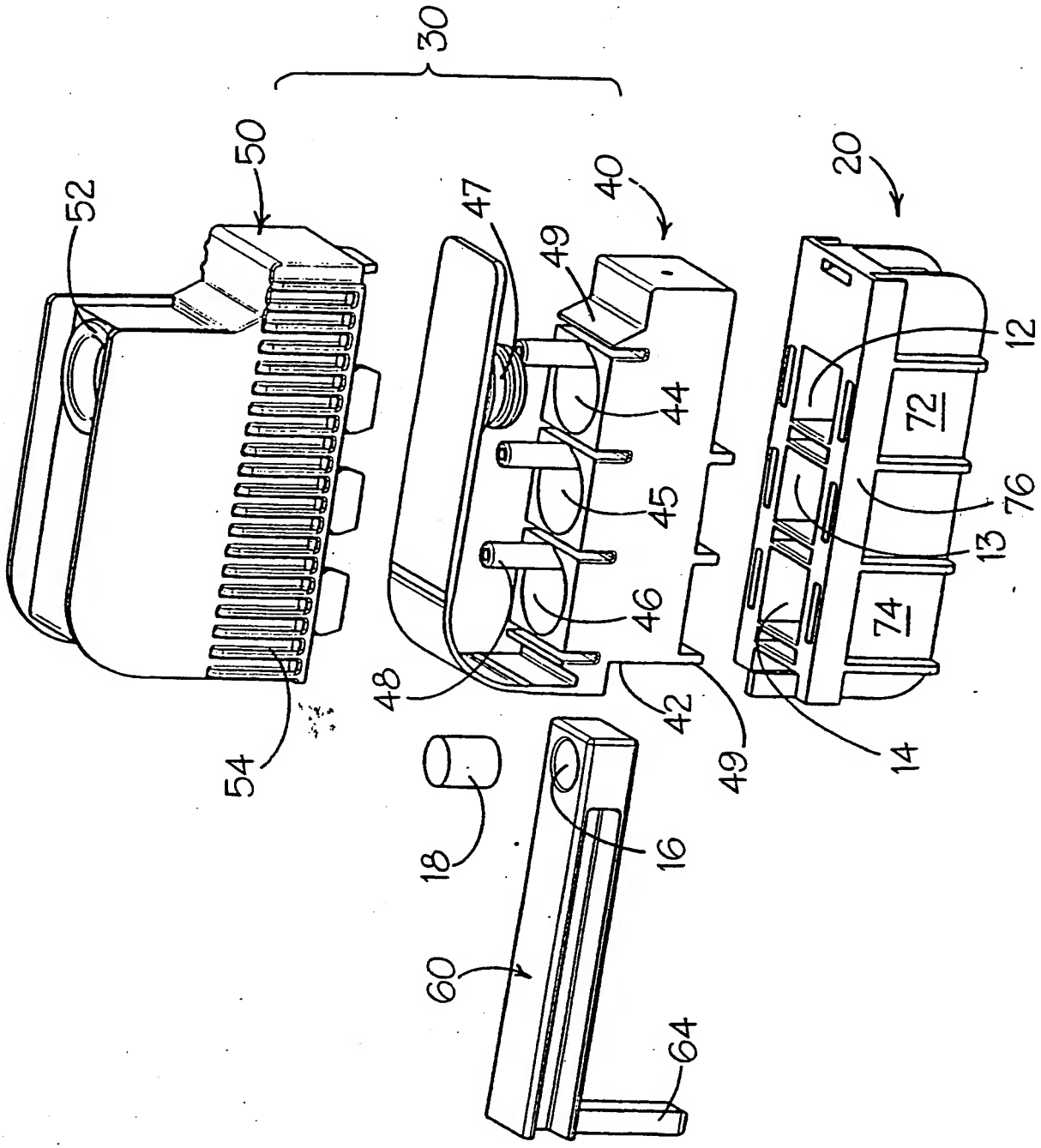


FIG. 2.

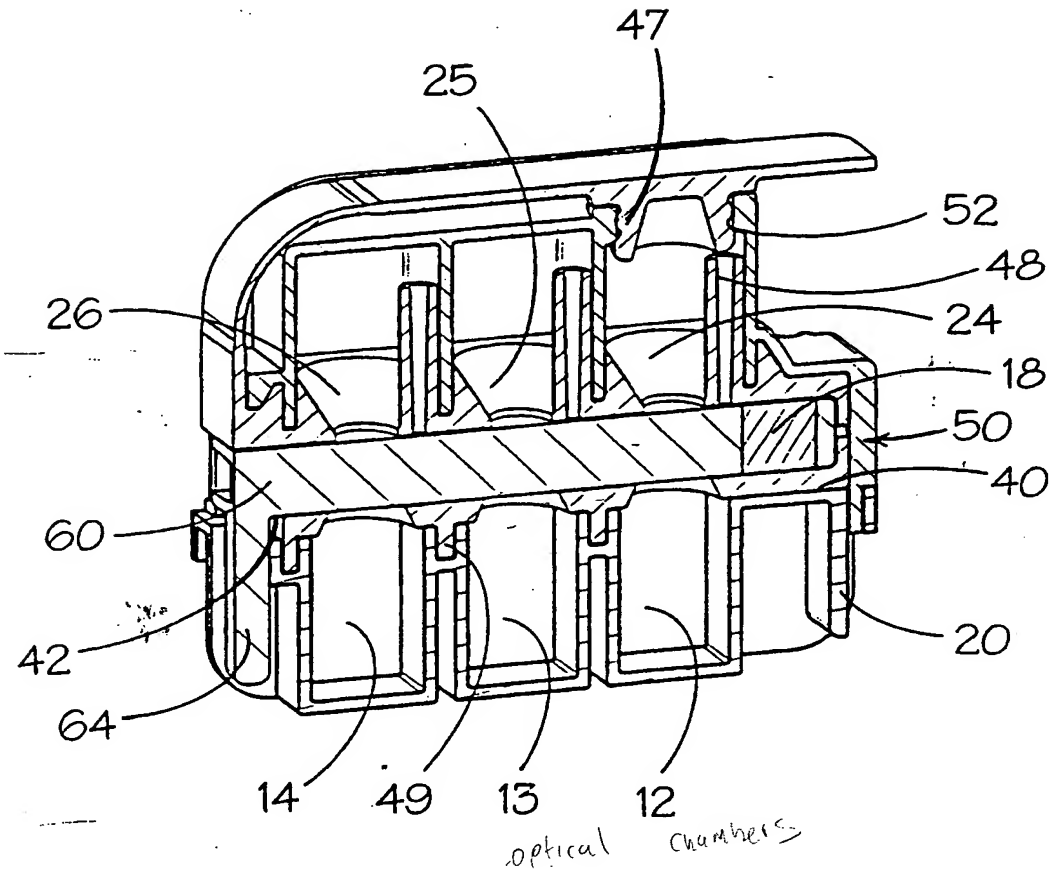


FIG. 3.

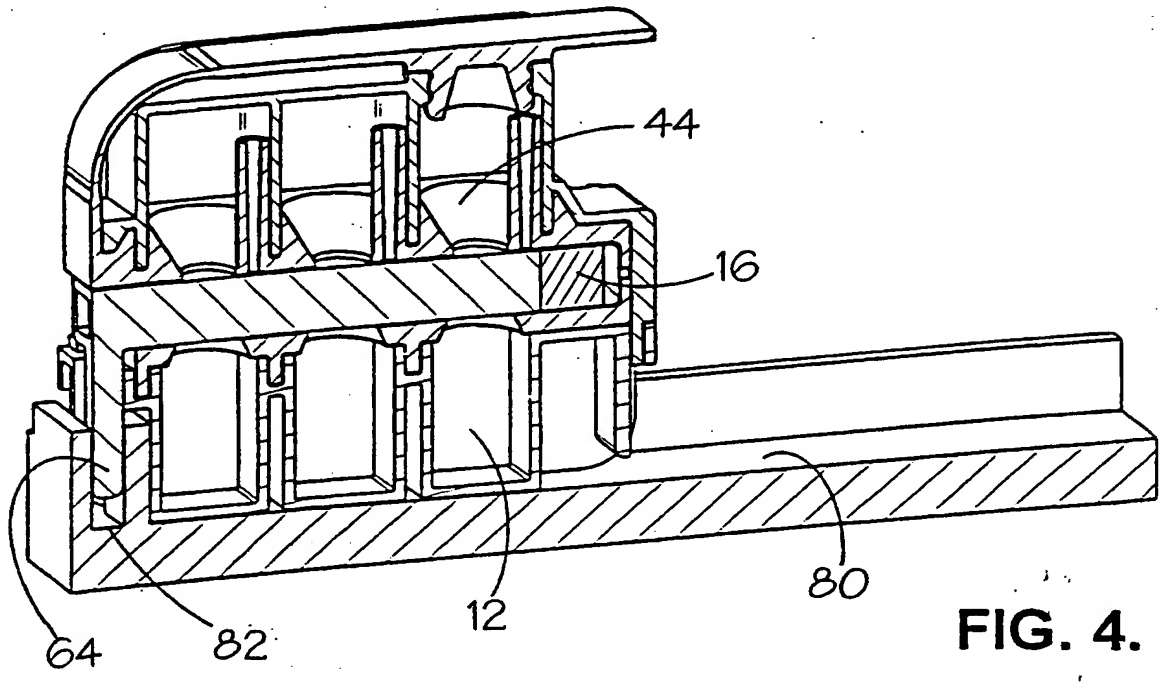


FIG. 4.

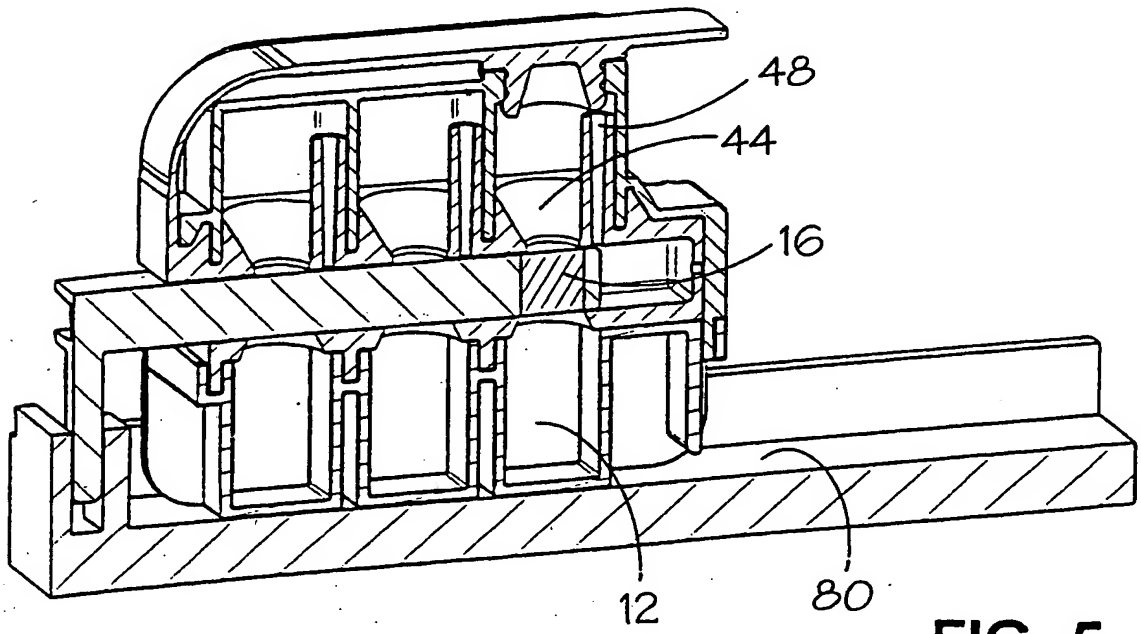


FIG. 5.

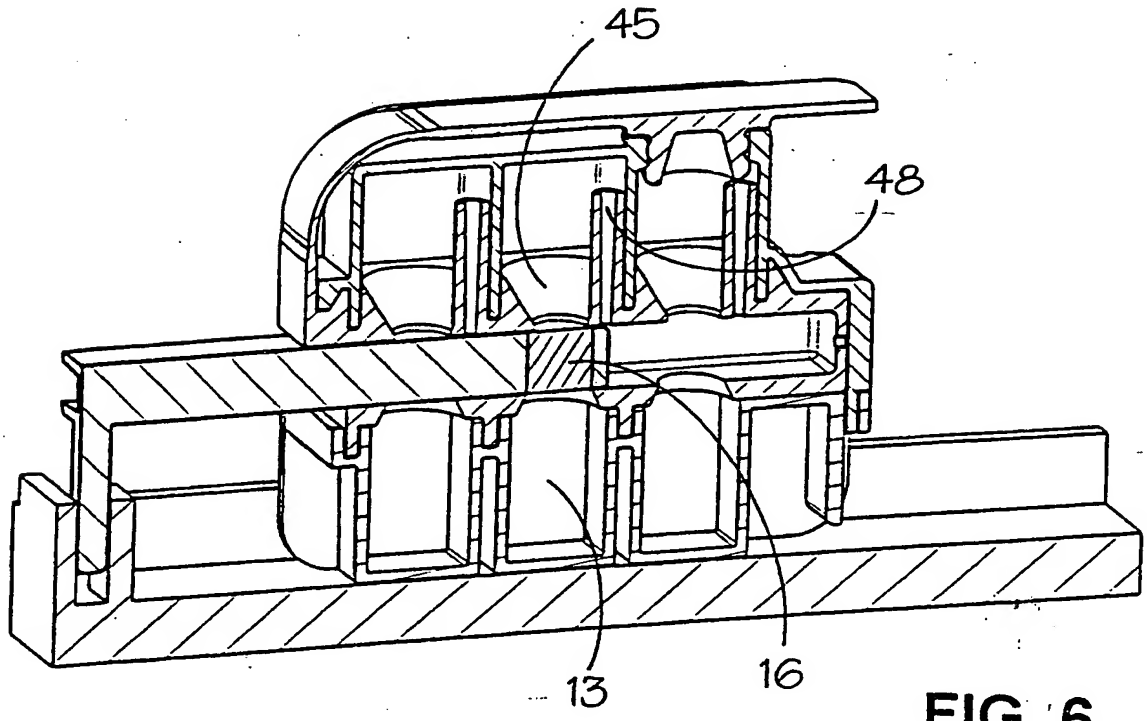


FIG. 6.

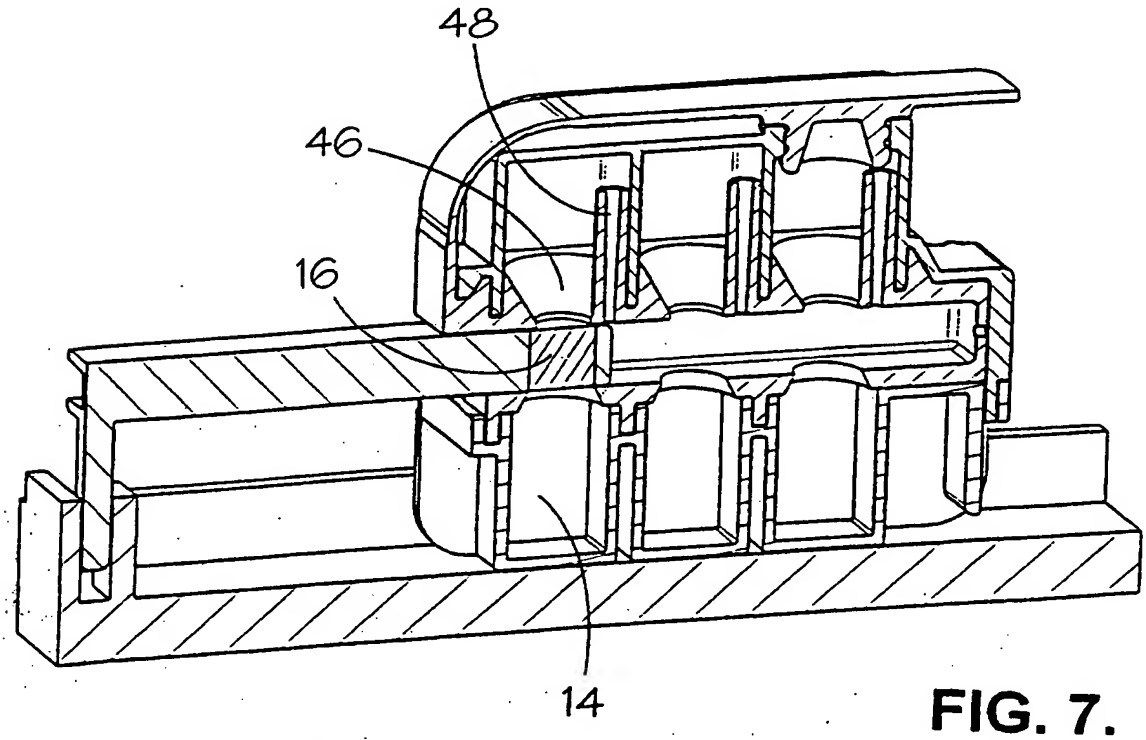


FIG. 7.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter[illegible]pplication No
PCT/GB 00/02251

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4482251 A	13-11-1984	NONE	
WO 9112515 A	22-08-1991	US 5073029 A	17-12-1991
		AU 7313791 A	03-09-1991
		EP 0515526 A	02-12-1992
		JP 5504624 T	15-07-1993
US 3523737 A	11-08-1970	NONE	
EP 0353025 A	31-01-1990	US 4877586 A	31-10-1989
		CA 1332911 A	08-11-1994
		DE 68906479 D	17-06-1993
		JP 2074863 A	14-03-1990
US 3837746 A	24-09-1974	US 3837745 A	24-09-1974
		BE 805119 A	16-01-1974
		CA 1024049 A	10-01-1978
		CA 1023970 A	10-01-1978
		CA 1024217 A	10-01-1978
		DE 2347173 A	18-04-1974
		DE 2365297 A	13-02-1975
		DK 263978 A	13-06-1978
		DK 264078 A	13-06-1978
		ES 418899 A	01-09-1976
		ES 425523 A	01-11-1976
		FR 2212939 A	26-07-1974
		GB 1445397 A	11-08-1976
		GB 1445398 A	11-08-1976
		GB 1445396 A	11-08-1976
		IL 43256 A	30-04-1978
		JP 1059730 C	25-08-1981
		JP 54015790 A	05-02-1979
		JP 55050292 B	17-12-1980
		JP 1032130 C	29-01-1981
		JP 49125093 A	29-11-1974
		JP 55020183 B	31-05-1980
		JP 54000689 A	06-01-1979
		NL 7312907 A,B,	22-03-1974
		SE 411254 B	10-12-1979
		SE 7709627 A	26-08-1977
		SE 7709628 A	26-08-1977
		US RE28801 E	04-05-1976
		AU 6045173 A	20-03-1975
		US 3938049 A	10-02-1976
		US 3983006 A	28-09-1976
		US 4013368 A	22-03-1977
		US RE28800 E	04-05-1976
		ZA 7307401 A	25-09-1974
US 5800784 A	01-09-1998	AU 3653297 A	10-02-1998
		CA 2259648 A	29-01-1998
		EP 1015881 A	05-07-2000
		WO 9803264 A	29-01-1998
		US 6039924 A	21-03-2000
		US 6082417 A	04-07-2000
		US 5918273 A	29-06-1999

INTERNATIONAL SEARCH REPORT

Inte Application No
PCT/GB 00/02251

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01L3/00 G01N21/25 G01N35/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01L G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, EPO-Internal, INSPEC, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 482 251 A (SAYLOR RICHARD) 13 November 1984 (1984-11-13) column 1, line 7 - line 26 column 2, line 3 - line 63; figure 1 ---	22,23
X	WO 91 12515 A (EQM RES INC) 22 August 1991 (1991-08-22) page 10, line 2 - line 6 page 10, line 17 - line 19 page 11, line 11 - line 12 page 14, line 12 - line 13 page 20, line 27 -page 21, line 34; figure 5 --- -/--	22,23

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 August 2000	28/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Skalla, J

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 523 737 A (WOOD WILLIS AVERY ET AL) 11 August 1970 (1970-08-11) column 1, line 33 -column 2, line 47 column 5, line 65 -column 6, line 28; figures 1,2	22,23
A	EP 0 353 025 A (EASTMAN KODAK CO) 31 January 1990 (1990-01-31) column 1, line 8 -column 2, line 21 column 3, line 23 -column 5, line 21; figures 3,4	1,2
A	US 3 837 746 A (ACKER J ET AL) 24 September 1974 (1974-09-24) column 1, line 12 - line 54 column 2, line 43 -column 3, line 47 column 5, line 35 - line 38 column 6, line 1 - line 12 column 9, line 1 - line 3	1-3, 14-16, 19,22,23
A	US 5 800 784 A (HORN MARCUS J) 1 September 1998 (1998-09-01) column 10, line 63 -column 12, line 23	1,2

mb

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
P400545WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/ 02251	09/06/2000	10/06/1999
Applicant		
PROVALIS DIAGNOSTICS LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [X] as suggested by the applicant.

   [ ] None of the figures.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

PA NT COOPERATION TREAT

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 20 February 2001 (20.02.01)	
International application No. PCT/GB00/02251	**Applicant's or agent's file reference** P400545WO
International filing date (day/month/year) 09 June 2000 (09.06.00)	**Priority date** (day/month/year) 10 June 1999 (10.06.99)
Applicant ANDREWES, David et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

04 January 2001 (04.01.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Olivia TEFY

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

W.P. THOMPSON & CO.
Coopers Building
Church Street
Liverpool L1 3AB
GRANDE BRETAGNE

RECEIVED 28 AUG 2001

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	23.08.2001
Applicant's or agent's file reference P400545WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02251	09/06/2000	10/06/1999

Applicant
PROVALIS DIAGNOSTICS LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Conner, M Tel.+49 89 2399-2241

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P400545WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02251	09/06/2000	10/06/1999
International Patent Classification (IPC) or national classification and IPC B01L3/00		
Applicant PROVALIS DIAGNOSTICS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04/01/2001	23.08.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Skalla, J Telephone No. +49 89 2399 2252

Form PCT/IPEA/409 (cover sheet) (January 1994)

II ERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02251

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-10 as originally filed

Claims, No.:

1-24 as originally filed

Drawings, sheets:

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-21,24.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-21,24 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☒ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims

	No:	Claims	22,23
Inventive step (IS)	Yes:	Claims	
	No:	Claims	22,23
Industrial applicability (IA)	Yes:	Claims	22,23
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

1. Cited documents

Reference is made to the following documents mentioned in the international search report:
D1: EP-A-0 353 025,
D2: US-A-4 482 251,
D3: WO-A-91 12515,
D4: US-A-3 523 737.
Documents D1 and D3 had also been cited in the search report corresponding to the application WO-A-99 28038 which is acknowledged in the description on page 1.

2. Remarks with respect to item III

In view of the clarity objections, an examination of claims 1-21 and 24 with respect to novelty and inventive step is not possible. However, it is noted that these claims prima facie appear to fulfil the novelty and inventive step requirements if these objections can be met, the reasons being as follows:

The invention relates to an apparatus for conducting an assay.
Document D1 may be considered as the most pertinent prior art because it discloses an apparatus for use in an assay, wherein an inlet port (namely the bottoms 53 of wells) can be brought into liquid communication with respective inlets to chambers which are filled with an absorbent material (66). The bottom of each well is provided with a filter and blocked either by a liquid lock or some other means. Both wells and filters are carried on an upper housing. In use the upper housing slides relative to the lower housing which is kept stationary (or vice versa).
It is a problem with said device that the filter is locked to the upper housing and cannot be removed therefrom without moving the upper housing.
It may be considered as an object of the invention to overcome this problem.
Bearing in mind the clarity objections, this appears to be achieved by arranging an inlet port accommodating a filter or binder retaining means in a movable component which can be brought into liquid communication with each inlet to the chambers in turn as required such that liquid can flow via the inlet port into the respective inlet, and which is moved along a linear path between a sample receiving chamber and the chambers comprising the respective inlet ports.

These additional features would not be hinted at by any available prior-art document.

3. Remarks with respect to item V

Lack of novelty (Art. 33(2) PCT) of claims 22 and 23:

The features of claims 22 and 23 are already disclosed in documents D2 and D3 and do at least not appear to be inventive in view of document D4.
In particular, reference is made to D4, Fig. 2 and col. 6, l. 17-27 disclosing an arrangement which moves an apparatus (an array of cuvettes which are arranged in a line for the purpose of successive examination) on an elongate track (the cuvette carrier) into a reading position.
See also D2, Fig. 1 and col. 2, l. 3-38 disclosing a shuttle motor bringing the cuvettes into a reading position, and D3, abstract and Fig. 5. The device of D3 discloses the use of several light detectors and receivers, see p. 20, l. 27-31. D3 also mentions the use of an optical cutoff filter (8). A filter is also depicted in D2, Fig. 1. D4 mentions the necessity to adjust the wavelength to specific selected values, see col. 2, l. 27-37. A person skilled in the art would contemplate using a filter for this purpose.
A power source, an analogue-to-digital converter and a microprocessor operable via a key pad are common design features, see also D3, p. 10, l. 3-6, l. 17-19, p. 11, l. 11-12 and p. 14, l. 12-13 and D2, Fig. 1 disclosing A/D converter and keyboard.

Thus, claims 22 and 23 are not new.

It is noted that the definition of an apparatus presenting a sample is vague. For the above comparison of the claims with the prior art, it has been considered that an array of cuvettes is also an apparatus because it comprises several appliances arranged for a specific purpose. The claims would not become inventive by defining that any means used for filling the cuvettes or causing assay reactions are moved together with the cuvettes. The cuvettes of D2-D4 are used for clinical and/or chemical purposes. In accordance with circumstances, a person skilled in the art would contemplate arranging any device on the track, which is suitable for filling the cuvettes or for causing reactions within the cuvettes.

4. Remarks with respect to item VII

4.1 In contrast to the requirements set out in Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1 is not mentioned in the description. Document D1 is relevant insofar as it discloses an apparatus for use in an assay, wherein an inlet port can be brought into liquid communication with an inlet to a chamber, see e.g. Fig. 4 and corresponding description in col. 3, l. 42 - col. 4, l. 23. The inlet port comprises a filter membrane to separate out free, unreacted immunoreagents.

4.2 On page 8, first paragraph, the "second component 60" should have been replaced by 'the third component'.
Moreover, the reference numeral "78" of the projecting fins is not included in the drawings.

4.3 The international application number mentioned on p. 1, second paragraph is wrong and should read 'PCT/GB98/03586'.

5. Remarks with respect to item VIII

5.1 It appears that the first and the second "inlet" mentioned in claim 1 relate to the openings of respective chambers.

5.2 The expression "liquid communication" in claim 1 is vague and in view of Fig. 3-7 it appears that *'the inlet port can be brought into liquid communication with each inlet in turn as required, such that liquid can flow via the inlet port into the respective inlet'*.
Moreover, the existence of a movable inlet port necessitates the existence of a component ('third component') comprising this inlet port. This feature is essential to the performance of the invention.
Bearing in mind that claim 1 is addressed to an apparatus presenting a sample, a sample receiving means must be present which in the present case is represented by a sample receiving chamber, the third component being moved between sample receiving chamber and the chambers comprising the first and second inlets, respectively.

5.3 It is not clear which features are actually added by the definition of a cartridge in

claim 2 because no specific shape or size of the cartridge are indicated.

5.4 Several of the claims list components of the apparatus without defining the relative arrangement and/or the function of the these components. Consequently, the claims would cover a variety of arrangements not supported by the description.
This objection applies to the following claims:

Claim 3: It is not defined how the first, second and third components are arranged in relation to each other. Moreover, it appears that not the inlets include optical chambers but rather the chambers have inlets. The expression "optical chambers" has no well-established meaning giving the reader a clear instruction about the function of the chambers.

Claims 6, 8 and 16: The location and function of the "additional sealing means" and the "resilient component" are not defined, respectively.

Claims 9 and 14: The function of the "plug closure" and the "air relief tubes" are not defined, respectively.

Claim 19: The function of the "windows" is not indicated.

Claim 22: The function and location of the light emitters and detectors, the "driver" and the A/D converter are not defined.

5.5 The expression "clear material" used in claim 15 is vague. (Probably it is meant that the material is translucent.)

5.6 The "resilient component" mentioned in claim 17 has no antecedent in all possible claimed combinations of claims, on which claim 17 is dependent.

5.7 Claim 18 mentions "the slide" which has no antecedent. Also "the chamber" and "the chamber contents" are not defined. The same objection applies to "the main apparatus surface" in claim 19.

5.8 For comparison of claim 22 with the prior art, it has been considered that the

instrument comprises an elongate track 'adapted to bring *the* apparatus into a reading position'.

5.9 The function of the device of claim 24 is not indicated.